

REMARKS

Claims 1, 17 and 27-45 are presently pending. Claims 1, 17 and 27 have been amended to correct a typographical error in the spelling of the term “infarction.” Support for these amendments is found in the specification at least at page 20, line 30.

New claims 28-45 have been added. Support for new claims 28-45 is found in the specification at least at page 20, line 18 to page 21, line 4.

No new matter has been added. Applicant reserves the right to prosecute the subject matter of any canceled, amended or withdrawn claim, or any other unclaimed subject matter, in one or more continuation, divisional or continuation-in-part applications.¹

I. The Rejections Under 35 U.S.C. §112, First Paragraph

Claims 1, 17 and 27 are rejected under 35 U.S.C. §112, first paragraph, for being allegedly indefinite. In particular, while acknowledging that claims 1, 17 and 27 are enabled with respect to “inhibition of the JNK pathway,” the Examiner has stated that the conditions recited therein are not enabled. Applicant respectfully traverses this rejection.

The test for enablement is whether or not any person skilled in the art could make and use the invention from the disclosure in an application, coupled with information known in the art, without undue experimentation. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). Applicant submits that the present specification teaches how to make the compounds recited in the present method claims (at least at page 12, line 1 to page 16, line 23), teaches how to prepare the compounds for pharmaceutical administration (*i.e.*, compositions and dosages suitable for administration) (at least at page 21, lines 13-32), teaches how to administer the compounds (at least at page 21, line 33 to page 22, line 6) and teaches diseases possessed by patients in need of administration (at least at page 5, line 31 to page 6, line 15). Nothing more is legally required to enable the claims. However, in order to be fully responsive, Applicant has addressed the Examiner’s specific concerns below.

The Examiner states that the nature of the invention is extremely complex in that it encompasses a vast array of unrelated conditions. Applicant respectfully submits that the conditions recited in the claims are in fact related because each is associated with the JNK

¹ Applicant notes that in a June 2, 2005 teleconference with Examiner Richard L. Raymond in connection with co-owned U.S. Application No. 10/004,642 (the “’642 application”), Examiner Raymond agreed to withdraw a provisional obviousness-type double patenting rejection in the ’642 application over the present application because the provisional obviousness-type double patenting rejection was the sole remaining rejection in the ’642 application and the present application has not yet been allowed.

pathway. The JNK pathway touches on numerous and diverse disease settings, some of which may not normally be thought of as being related. Enclosed herewith is a copy of a peer-reviewed literature publication which states that “JNK activity seems critical for both immune response and for programmed cell death. Therapeutic inhibition of JNK may provide clinical benefit in diseases as diverse as arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease, graft vs. host disease, stroke, Parkinson’s disease, ischemic injury, and myocardial infarction.” Bennett *et al.*, *P.N.A.S.* 98(24):13681-13686 (2001) (submitted herewith as reference DH on the accompanying List of References Cited by Applicant). Thus, the JNK pathway is associated with numerous diseases, including cancer, inflammatory diseases and cardiovascular diseases. Applicant submits the following additional peer-reviewed publications that demonstrate the correlation between particular claimed diseases and the JNK pathway:

(1) Bennett, *et al.*, *P.N.A.S.* 98(24):13681-13686 (2001) (submitted herewith as reference DH on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in, *inter alia*, cancer, graft vs. host disease, ischemia/reperfusion injury and myocardial infarction (see page 13686, first column, lines 23-26 and page 13686, second column, lines 6-7 and 27-30);

(2) Downey, *et al.*, *Frontiers in Bioscience* 3:468-476 (1998) (submitted herewith as reference DI on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in multiple organ failure and septic/endotoxin shock (see page 468, Abstract);

(3) Haunstetter, *et al.*, *Circ. Res.* 82:1111-1129 (1998) (submitted herewith as reference DJ on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in apoptosis (see page 1119, second column, lines 21-22) which is critically involved in cardiovascular diseases, including atherosclerosis (see page 1120, second column, first paragraph of section 8 and Table 4);

(4) Hreniuk, *et al.*, *Molecular Pharmacology* 59(4):867-874 (2001) (submitted herewith as reference DK on the accompanying List of References Cited by Applicant): teaches that inhibition of the JNK pathway may be useful for preventing reperfusion injury (see page 874, last paragraph);

(5) Izumi, *et al.*, *Hypertension* 36:511-516 (2000) (submitted herewith as reference DL on the accompanying List of References Cited by Applicant): teaches that JNK is involved in cardiac hypertrophy (see page 511, last sentence of Abstract);

(6) Kim, *et al.*, *J. Pharmacol. Sci.* 91:177-181 (2003) (submitted herewith as reference DM on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in cardiovascular disease and restenosis following angioplasty²;

(7) Purves, *et al.*, *FASEB* 15:2508-2514 (2001) (submitted herewith as reference DN on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in diabetes, including Type II diabetes (see page 2508, Abstract); and

(8) Srivastava, *et al.*, *J. Clin. Invest.* 104(4):503-513 (1999) (submitted herewith as reference DO on the accompanying List of References Cited by Applicant): teaches that the JNK pathway is involved in osteoclast formation and bone loss (*i.e.*, osteoporosis) because decreased JNK activity decreases TNF α production (see page 504, first column, lines 15-18) and TNF α production is responsible for osteoclast formation and bone loss (see page 512, last paragraph).

Accordingly, Applicant respectfully submits that the claimed diseases are indeed related because each is associated with the JNK pathway.

The Examiner has further stated that the specification does not give adequate guidance as to the actual treatment of the claimed conditions, does not provide working examples of such treatment, and that a greater amount of evidence is required to show its operability in humans. Applicant submits that such guidance and working examples are not requirements for patentability and neither is a showing of operability in humans. The Federal Circuit has held that it is not necessary to enable one skilled in the art to make and use a perfected, commercially viable embodiment in order to satisfy the enablement requirement. *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338 (Fed. Cir. 2003). Indeed, an Applicant need not even demonstrate that an invention is completely safe to satisfy the requirements of 35 U.S.C. § 112. M.P.E.P. § 2164.01(c). The PTO should be wary not to overstep its role in examining patent applications. Indeed, the Federal Circuit has specifically stated that it is the Food and Drug Administration and not the PTO that determines the safety and efficacy of drugs for use in humans. *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995) (Testing for the full safety and effectiveness ... is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the

² Applicant notes that the authors of reference DL are also authors of the Yano reference cited by the Examiner. These authors cite Yano in the first paragraph of page 178 of reference DL in part for the proposition that MAP kinases are activated in hypertrophied heart, balloon-injured artery, and hypertensive vascular or renal tissue and state that, accordingly, "it is *assumed* that MAP kinases may be involved in cardiovascular and renal diseases" (emphasis added).

confines of Patent and Trademark Office (PTO) proceedings). This regulatory process is not the same as the enablement requirement under 35 U.S.C. § 112. Furthermore, the Federal Circuit has clearly stated that the operability of a claimed invention is a different inquiry than whether the claim is enabled by the specification. *National Recovery Technologies, Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999). Indeed, a claim is not invalid for lack of operability because the invention does not work perfectly under all conditions.³ *Id.*

The Examiner has further stated that undue experimentation would be required to practice the claimed invention at least in part because if a particular carrier, dosage, duration of treatment and animal model was unsuccessful, it would have to be modified and tested again. Applicant submits that experimentation by definition is the process of modifying and testing again. The correct inquiry is whether or not in the instant case the experimentation is undue. It is well-established that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, (Fed. Cir. 1985); M.P.E.P. § 2164.01. Applicant respectfully submits that physicians routinely perform the tasks of determining dosage amounts and routes of administration regularly every day. Indeed, the Federal Circuit has held that a specification is enabling in part because those skilled in the art would know how to conduct a dose response study to determine the appropriate amounts to be used. *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989). Accordingly, Applicant respectfully submits that it would not require undue experimentation to treat the claimed diseases with the claimed compounds, which have been shown to be JNK inhibitors.

The Examiner has pointed to Yano *et al.*, *Circ. Res.* 83:752-760 (1998) ("Yano") for the proposition further study is needed to elucidate the role of JNK involvement in cardiac hypertrophy. As discussed above in footnote 1, certain authors of Yano subsequently published a related paper wherein Yano was cited for the proposition that "it is assumed that MAP kinases may be involved in cardiovascular and renal diseases." Thus, Applicant submits that the Examiner's reliance on Yano is improper. Nevertheless, Applicant

³ Even assuming for the sake of argument that some of the compounds of the present claims are not effective against all claimed diseases, it is well-settled that the "presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled." M.P.E.P. § 2164.08(b).

respectfully submits that elucidating JNK's role in the claimed diseases (*e.g.*, cardiac hypertrophy) is not necessary and that evidence of JNK's role in the claimed diseases is what is relevant. The Federal Circuit has held that an inventor does not need to comprehend the scientific principles upon which an invention is based, nor is an inventor's theory or belief as to how an invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. §112. *Cross v. Iizuka*, 753 F.2d 1040, 1042 (Fed. Cir. 1985).

Notably, in a non-precedential opinion the Board of Patent Appeals and Interferences reversed a rejection under 35 U.S.C. §112, first paragraph, of a claim directed to the treatment of atherosclerosis wherein Applicant demonstrated that the claimed compounds had estrogenic activity and it was known in the art that estrogenic compounds were useful for treating atherosclerosis. *Ex Parte Raveendranath*, 1995 WL 1768438 (B.P.A.I. 1995) (a copy enclosed). In particular, the Board stated "the specification disclosure as to the estrogenic activity of the claimed compounds would have enabled those skilled in the art to use the claimed compounds for the treatment of estrogen-related disorders and atherosclerosis." *Id.*

Finally, Applicant notes that the claimed invention is directed to uses of a specific class of compounds. Thus, the invention is limited to specific uses of specific compounds and is not extremely complex as suggested by the examiner. Applicant submits that the present specification discloses and demonstrates that claimed compounds are useful as JNK inhibitors and, in view of the references submitted herewith, that it is known that the JNK pathway is associated with the claimed diseases. Accordingly, Applicant submits that claims 1, 17 and 27-45 satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

In view of the above remarks, it is believed that the rejection of claims 1, 17 and 27 under 35 U.S.C. §112, first paragraph, cannot stand and must be withdrawn.

Conclusion

Applicant respectfully requests that the present amendments be entered and the present remarks be made of record in the file history of the present application. An early allowance of the application is earnestly requested. The Examiner is invited to call the undersigned with any questions concerning the foregoing.

No fee other than those for filing of the Third Supplemental Information Disclosure Statement and the Petition for Extension of Time are believed to be due in connection with this response; however, should any other fee be required, Applicant hereby authorizes that the required fee be charged to Jones Day Deposit Account No. 50-3013.

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Respectfully submitted,

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